

**WE CLAIM:**

1. In a device having a sample vessel for processing and/or analyzing a sample molecule, the improvement comprising employing:

- 5           a reservoir holding a fluid sample comprised of the sample molecule;  
          an ejector comprising an acoustic radiation generator for generating acoustic radiation and a focusing means for focusing the acoustic radiation at a focal point near the surface of the fluid sample; and  
          a means for positioning the ejector in acoustic coupling relationship to the  
10       reservoir to eject a droplet of the fluid sample into the sample vessel.

2. The device of claim 1, wherein the sample vessel is an ionization chamber.

3. The device of claim 2, wherein the device is a mass spectrometer.

15           4. The device of claim 3, wherein the mass spectrometer is a time-of-flight mass spectrometer.

20           5. The device of claim 1, wherein the fluid sample occupies a volume of no more than about 100  $\mu$ L.

          6. The device of claim 5, wherein the fluid sample occupies a volume of no more than about 10  $\mu$ L.

25           7. The device of claim 6, wherein the fluid sample occupies a volume of no more than about 1  $\mu$ L.

          8. The device of claim 7, wherein the fluid sample occupies a volume of about 10 pL to about 100 nL.

-49-

9. The device of claim 1, wherein the ejector is configured to eject a droplet having a volume of no more than about 1 nL.

10. The device of claim 9, wherein the ejector is configured to eject a droplet having a volume of no more than about 1 pL.

11. The device of claim 10, wherein the ejector is configured to eject a droplet having a volume of no more than about 100 fL.

12. The device of claim 1, wherein the ejector is configured to eject no more than about 5 percent of the fluid sample per droplet.

13. The device of claim 1, wherein the sample molecule has a molecular weight of about 100 daltons to about 100 kilodaltons.

14. The device of claim 13, wherein the molecular weight is about 1 to about 100 kilodaltons.

15. The device of claim 1, wherein the fluid sample further comprises water.

16. The device of claim 1, wherein the sample molecule is nonmetallic.

17. The device of claim 16, wherein the sample molecule is an organic compound.

18. The device of claim 17, wherein the organic compound is a biomolecule.

19. The device of claim 18, wherein the biomolecule is nucleotidic

20. The device of claim 18, wherein the biomolecule is peptidic.

21. The device of claim 1, further comprising a detector for detecting reflected acoustic radiation from the fluid sample.

5           22. The device of claim 2, further comprising a charging means for electrically charging the fluid sample.

23. The device of claim 22, wherein the charging means is configured to electrically charge the surface of the fluid sample.

10           24. The device of claim 22, wherein the charging means is configured to electrically charge the entire fluid sample.

25. The device of claim 22, further comprising a charged surface within the ionization chamber that attracts or repels the droplet.

15           26. The device of claim 25, wherein the charged surface is a surface of a multipole analyzer.

20           27. The device of claim 26, wherein the multipole analyzer is a quadrupole analyzer.

28. The device of claim 2, wherein the reservoir is located within the ionization chamber.

25           29. The device of claim 1, wherein the sample vessel comprises a microfluidic device.

30           30. The device of claim 1, wherein the sample vessel represents a portion of a microfluidic device.

-51-

31. The device of claim 30, wherein the reservoir represents a portion of an additional microfluidic device.

32. A method for introducing a sample molecule into a sample vessel of a device for processing and/or analyzing a sample molecule, comprising:

(a) providing a reservoir holding a fluid sample comprised of the sample molecule; and

(b) directing focused acoustic radiation at a point near the surface of the fluid sample to eject a droplet of the fluid sample from the surface of the fluid sample along a predetermined trajectory into the sample vessel of the device.

33. The method of claim 32, wherein the sample vessel is an ionization chamber.

34. The method of claim 33, wherein the device is a mass spectrometer.

35. The method of claim 34, wherein the mass spectrometer is a time-of-flight mass spectrometer.

36. The method of claim 32, further comprising repeating step (b).

37. The method of claim 36, wherein the ejected droplets are substantially identical in size.

38. The method of claim 36, wherein no more than about 5 percent of the sample fluid is ejected per droplet.

39. The method of claim 36, wherein the predetermined trajectories of the ejected droplets are substantially identical.

-52-

40. The method of claim 33, wherein the predetermined trajectory intersects an electric field.

5 41. The method of claim 32, wherein the sample molecule has a molecular weight of about 100 daltons to about 100 kilodaltons.

42. The method of claim 41, wherein the molecular weight is about 1 to about 100 kilodaltons.

10 43. The method of claim 33, wherein the sample molecule has a molecular weight to charge ratio of about 100 daltons/charge to about 100 kilodaltons/charge

44. The method of claim 32, wherein the fluid sample further comprises water.

15 45. The method of claim 32, wherein the sample molecule is nonmetallic.

46. The method of claim 45, wherein the sample molecule an organic compound.

47. The method of claim 46, wherein the organic compound is a biomolecule.

20 48. The method of claim 47, wherein the biomolecule is nucleotidic.

49. The method of claim 47, wherein the biomolecule is peptidic.

25 50. The method of claim 32, further comprising, after step (a) and before step (b), (a') transmitting acoustic radiation through the fluid sample and detecting for reflected acoustic radiation.

30 51. The method of claim 33, further comprising, after step (a) and before step (b), (a') electrically charging the fluid sample.

52. The method of claim 51, wherein step (a') is carried out by charging the surface of the fluid sample.

5 53. The method of claim 51, wherein step (a') is carried out by charging the reservoir.

54. The method of claim 32, wherein the sample vessel comprises a microfluidic device.

10

55. The method of claim 32, wherein the sample vessel represents a portion of a microfluidic device.

15

56. The method of claim 55, wherein the reservoir represents a portion of an additional microfluidic device.

20

57. In a device having a sample vessel for processing and/or analyzing a plurality of sample molecules, the improvement comprising employing:

a plurality of reservoirs each holding a fluid sample comprised of a sample molecule;

an ejector comprising an acoustic radiation generator for generating acoustic radiation and a focusing means for focusing the acoustic radiation at a focal point near the surface of the fluid sample; and

25

a means for positioning the ejector in acoustic coupling relationship to each of the reservoirs to eject a droplet of fluid sample into the sample vessel.

58. The device of claim 57, wherein the sample vessel is an ionization chamber.

59. The device of claim 57, wherein the device is a mass spectrometer.

30

-54-

60. The device of claim 57, wherein the reservoirs are arranged in an array.

61. The device of claim 57, wherein the reservoirs are provided as integrated members of a single substrate.

5

62. The device of claim 61, wherein the reservoirs comprise designated sites on a surface of the substrate surface.

63. The device of claim 62, wherein the substrate surface is substantially flat.

10

64. The device of claim 57, wherein at least one sample molecule is a biomolecule.

65. The device of claim 57, further comprising a detector for detecting reflected acoustic radiation from the fluid sample.

15

66. The device of claim 58, further comprising a charging means for electrically charging at least one fluid sample.

20

67. The device of claim 66, wherein the charging means is configured to electrically charge fluid samples in succession.

68. The device of claim 66, wherein the charging means is configured to electrically charge all sample fluids simultaneously.

25

69. The device of claim 58, further comprising a charged surface within the ionization chamber.

70. The device of claim 69, wherein the charged surface is a surface of a multipole analyzer.

30

71. The device of claim 70, wherein the multipole analyzer is a quadrupole analyzer.

5           72. The device of claim 57, wherein the device comprises 96 reservoirs.

73. The device of claim 72, wherein the device comprises 384 reservoirs.

74. The device of claim 73, wherein the device comprises 1536 reservoirs.

10

75. The device of claim 57, further comprising a means for altering the spatial relationship of at least one reservoir with respect to the sample chamber.

15

76. The device of claim 57, wherein the sample vessel comprises a microfluidic device.

77. The device of claim 57, wherein the sample vessel represents a portion of a microfluidic device.

20

78. The device of claim 77, wherein at least one of the plurality of reservoirs represents a portion of an additional microfluidic device.

79. A method for introducing fluid samples into a sample vessel of a device for processing and/or analyzing a sample molecule, comprising:

25

(a) providing a plurality of reservoirs each holding a fluid sample having a fluid surface;

(b) positioning an ejector in acoustically coupled relationship to a selected reservoir;



(c) activating the ejector to generate acoustic radiation having a focal point near the fluid surface of the fluid sample held in the selected reservoir to eject a droplet of fluid sample into the sample vessel; and

(d) optionally repeating steps (b) and (c) for an additional reservoir.

5

80. The method of claim 79, wherein the sample vessel is an ionization chamber.

81. The method of claim 79, wherein the sample vessel comprises a microfluidic device.

10

82. The method of claim 79, wherein the sample vessel represents a portion of a microfluidic device.

15

83. The method of claim 82, wherein at least one of the plurality of reservoirs represents a portion of an additional microfluidic device.

84. The method of claim 79, further comprising, before step (c), (b') locating the fluid surface of the fluid sample held by the selected reservoir.

20

85. The method of claim 84, wherein (b') is carried out by detecting reflected acoustic radiation from the fluid sample.

86. The method of claim 85, wherein step (a) comprises (a') filling the reservoirs with fluid samples.

25

87. The method of claim 86, wherein step (a') comprises acoustically ejecting fluid samples into the reservoirs.

88. A device for the efficient transport of a fluid sample, comprising:

-57-

a sample vessel having an inlet opening with a limiting dimension of no more than about 300  $\mu\text{m}$ ;

a reservoir holding a fluid sample having a volume of no more than about 5  $\mu\text{L}$ ;  
and

5 an ejector configured to eject at least about 25% of the fluid sample through the inlet opening into the sample vessel.

89. The device of claim 88 wherein the ejector comprises a radiation generator for generating radiation, a focusing means for directing the radiation at a focal point near  
10 the surface of the fluid sample, and a means for positioning the ejector in coupling relationship to the reservoir.

90. The device of claim 89, wherein the ejector does not directly contact the radiation generator.  
15

91. The device of claim 89, wherein the ejector is an acoustic ejector.

92. The device of claim 91, further comprising a coupling fluid interposed between the ejector and the reservoir for acoustic coupling.  
20

93. The device of claim 88, wherein the limiting dimension does not exceed about 100  $\mu\text{m}$ .

94. The device of claim 93, wherein the limiting dimension does not exceed  
25 about 50  $\mu\text{m}$ .

95. The device of claim 94, wherein the limiting dimension does not exceed about 20  $\mu\text{m}$ .

-58-

96. The device of claim 88, wherein the reservoir volume is no more than about about 1  $\mu$ L.

97. The device of claim 96, wherein the reservoir volume is no more than about  
5 100 nL.

98. The device of claim 97, wherein the reservoir volume is no more than about  
50 nL.

99. The device of claim 88, wherein the sample vessel has an interior volume of  
10 no more than about 5  $\mu$ L.

100. The device of claim 99, wherein the interior sample vessel volume is not  
more than about 1  $\mu$ L  
15

101. The device of claim 100, wherein the interior sample vessel volume is no  
more than about of about 100 nL.

102. The device of claim 101, wherein the interior sample vessel volume is no  
20 more than about 50 nL.

103. The device of claim 88, wherein the ejector is configured to eject at least  
about 50% of the fluid sample through the inlet opening into the sample vessel.

104. The device of claim 103, wherein the ejector is configured to eject at least  
25 about 75% of the fluid sample through the inlet opening into the sample vessel.

105. The device of claim 104, wherein the ejector is configured to eject at least  
about 85% of the fluid sample through the inlet opening into the sample vessel.  
30

-59-

106. The device of claim 88, wherein the sample vessel comprises a substantially flat surface and the inlet opening is located on the flat surface.

5 107. The device of claim 88, wherein the sample vessel comprises a capillary and the inlet opening provides access to an interior region of the capillary.

108. The device of claim 107, wherein the inlet opening is located at a terminus of the capillary.

10 109. The device of claim 108, wherein the interior region of the capillary is axially symmetric.

110. The device of claim 109, wherein at least a portion of the vessel is electrically conductive.

15 111. The device of claim 109, wherein at least a portion of the vessel is electrically insulating.

20 112. The device of claim 88, further comprising a field generation means for generating an electric field in the sample vessel.

113. The device of claim 88, further comprising a charging means for electrically charging the fluid sample.

25 114. The device of claim 88, wherein the sample vessel further comprises an outlet opening.

115. The device of claim 88, wherein the sample vessel comprises a microfluidic device.

-60-

116. The device of claim 88, wherein the sample vessel represents a portion of a microfluidic device.

5 117. The device of claim 116, wherein the reservoir represents a portion of a microfluidic device.

118. A method for the efficient transport of a droplet of a fluid sample comprising:

10 (a) providing a reservoir holding a fluid sample having a volume of no more than about 5  $\mu\text{L}$ ; and

(b) ejecting at least 25% of the fluid sample through an inlet opening of a sample vessel, wherein the inlet opening has a limiting dimension of no more than about 300  $\mu\text{m}$ .

15 119. The method of claim 118, wherein step (b) is carried out by directing focused acoustic radiation at a point near the sample fluid surface to eject a droplet of the fluid sample from the surface of the fluid sample through the inlet opening.

120. The method of claim 119, wherein step (b) is repeated.

20 121. The method of claim 118, wherein the droplet comprises a sample molecule that exits the sample vessel through an outlet opening.

122. The method of claim 118, wherein the droplet is electrically charged.

25 123. The method of claim 122, further comprising, before (b), (b') generating an electric field that intersects the predetermined trajectory.

124. The device of claim 118, wherein the sample vessel comprises a microfluidic device.

-61-

125. The device of claim 118, wherein the sample vessel represents a portion of a microfluidic device.

126. A method for preparing a plurality of sample molecules for analysis,  
5 comprising:

(a) preparing an array comprised of a plurality of sample molecules on a substrate surface by applying focused acoustic energy to each of a plurality of fluid-holding reservoirs, each of said reservoirs holding a sample molecule in a fluid to be applied to a designated site on the substrate surface; and

10 (b) successively applying sufficient energy to each site to ionize the sample molecules and release the sample molecules from the substrate surface for analysis.

127. The method of claim 126, wherein step (b) comprises bombarding at least one site with photons.

128. The method of claim 127, wherein photonic bombardment is carried out using a laser.

129. The method of claim 126, wherein step (b) comprises bombarding at least one site with electrons.

130. The method of claim 126, wherein step (b) comprises bombarding at least one site with ions.

131. The method of claim 126, wherein step (b) comprises heating at least one site.

132. The method of claim 126, wherein step (b) comprises directing focused acoustic energy to at least one site.

-62-

133. The method of claim 126, wherein step (b) comprises passing an electrical current through at least one site.

5 134. The method of claim 126, further comprising, after step (b), determining the mass of the ionized sample molecules.

135. A device for the efficient transport of a fluid sample, comprising:  
a sample vessel having an inlet opening with a limiting dimension of about 10  $\mu\text{m}$   
to about 300  $\mu\text{m}$ ;  
10 a reservoir holding a fluid sample having a depth of about 0.1 to about 30 times  
the limiting dimension of the inlet opening; and  
an ejector configured to eject a droplet of the fluid sample through the inlet  
opening into the sample vessel,  
wherein the sample vessel does not contact the fluid sample held by the reservoir.

15 136. A device for the efficient transport of a fluid sample, comprising:  
a sample vessel having an inlet opening with a limiting dimension no more than  
about 300  $\mu\text{m}$ ;  
a reservoir holding a fluid sample having a depth of about 0.1 to about 30 times  
20 the limiting dimension of the inlet opening; and  
an ejector configured to eject a droplet of the fluid sample through the inlet  
opening into the sample vessel,  
wherein the droplet has a diameter smaller than the limiting dimension of the inlet  
opening and further wherein the sample vessel does not contact the sample fluid held by  
25 the reservoir.

137. The device of claim 136, wherein the limiting dimension of the inlet opening is at least about 3  $\mu\text{m}$  greater than the diameter of the droplet.

-63-

138. The device of claim 136, wherein the limiting dimension of the inlet opening is no more than about 100 times the diameter of the droplet.

139. The device of claim 136, wherein the ejector is an acoustic ejector  
5 configured to eject a droplet of the fluid sample through the inlet opening into the sample vessel, comprising an acoustic radiation generator for generating acoustic radiation and a focusing means for focusing the acoustic radiation at a focal point near the surface of the fluid sample, and further wherein the acoustic ejector is in acoustic coupling relationship to the reservoir.

10 140. The device of claim 139, wherein the acoustic radiation generator is configured to generate a predetermined wavelength selected according to the limiting dimension of the inlet opening.

15 141. The device of claim 140, wherein the predetermined wavelength is no greater than the limiting dimension of the inlet opening.

142. The device of claim 141, wherein the predetermined wavelength is no greater than about 80% of the limiting dimension of the inlet opening.

20 143. The device of claim 139, wherein the predetermined wavelength is selected according to the depth of the fluid sample.

25 144. The device of claim 143, wherein the predetermined wavelength is no greater than about 80% of the depth of the fluid sample.

145. A method for preparing a sample surface for analysis, comprising:  
(a) providing a reservoir holding an analysis-enhancing fluid;  
(b) providing a sample surface in droplet-receiving relationship to the fluid  
30 holding reservoir; and



-64-

(c) applying focused acoustic energy in a manner effective to eject a droplet of the analysis-enhancing fluid from the reservoir such that the droplet is deposited on the sample surface at a designated site; and

(d) subjecting the sample to conditions sufficient to allow the analysis-enhancing fluid to interact with the sample surface to render the sample surface suitable for analysis.

146. The method of claim 145, wherein the analysis-enhancing fluid comprises an analysis-enhancing moiety and a carrier fluid.

147. The method of claim 145, wherein the carrier fluid is evaporated from the sample surface in step (d).

148. The method of claim 145, wherein the analysis-enhancing fluid is solidified on the sample surface in step (d).

149. The method of claim 145, wherein the analysis-enhancing fluid comprises a mass-spectrometry matrix material.

150. The method of claim 149, wherein the mass-spectrometry matrix material is a photoabsorbing matrix material.

151. The method of claim 145, wherein step (c) is repeated such that a plurality of droplets is deposited on the sample surface.

152. The method of claim 141, wherein the plurality of droplets is deposited on the sample surface at the same designated site.

153. The method of claim 141, wherein the plurality of droplets is deposited on the sample surface at different designated sites.

154. The method of claim 143, wherein the different designated sites form an array.

5 155. The method of claim 151, wherein step (a) comprises providing a plurality of reservoirs each holding a different analysis-enhancing fluid and step (c) comprises applying focused acoustic energy in a manner effective to eject a droplet of fluid from each reservoir such that the droplets are deposited on the sample surface.

10 156. The method of claim 145, further comprising, after step (d), (e) applying sufficient energy to the designated site to ionize and release the sample molecules from the sample surface for analysis.

15 157. The method of claim 156, wherein step (e) comprises bombarding the designated site with photons.

158. The method of claim 157, wherein photonic bombardment is carried out using a laser.

20 159. The method of claim 156, further comprising, after step (e), (f) determining the molecular weight of the ionized sample molecules.

160. An apparatus for ejecting a fluid droplet from a microfluidic device, comprising:

25 a microfluidic device, comprising  
a base having a microchannel formed in a surface thereof, and  
a cover plate arranged over the base surface, the cover plate in combination with the microchannel defining a microconduit, wherein the microconduit fluidly communicates with an inlet opening and an outlet opening;

-66-

an ejector comprising an acoustic radiation generator for generating acoustic radiation and a focusing means for focusing the acoustic radiation at a focal point near the surface of a fluid at the outlet opening of the microfluidic device; and

5 a means for positioning the ejector in acoustic coupling relationship to the microfluidic device to eject a droplet from the outlet opening of the microfluidic device.

161. A method for ejecting a fluid droplet from a microfluidic device, comprising:

- 10 (a) providing a microfluidic device, comprising
- a base having a microchannel formed in a surface thereof, and
- a cover plate arranged over the base surface, the cover plate in combination with the microchannel defining a microconduit, wherein the microconduit fluidly communicates with an inlet opening and an outlet opening; and
- 15 (b) directing focused acoustic radiation at a point near the surface of a fluid at the outlet opening of the microfluidic device to eject a droplet of the fluid from the outlet opening of the microfluidic device.